

A marked-up version of the specification is provided to reflect the above changes.

In the "Brief Description of the Drawings":

~~FIG. 1 is a bar graph FIGS. 1A and 1B are bar graphs showing the survival of dissociated sympathetic neurons grown in collagen gels after 2 or 6 day treatments, respectively, with NT-3 (2 ng/ml) or GDNF (50 ng/ml), in the presence or absence of OP-1.~~

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

~~Please cancel, without prejudice, claim 24.~~

- b6 c4*
- B4*
1. (Twice Amended) A method for promoting survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:
contacting neural cells with an effective concentration of a preparation comprising
(a) an OP/BMP morphogen having an amino acid sequence at least 70% identical to the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone, and
(b) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6.

- b6 c5*
11. (Amended) A method as in claim 1, wherein said neural cells comprise neurons or neurological cells.

- b6 c6*
13. (Amended) A method as in claim 1, wherein said neural cells comprise peripheral nervous system cells.

B7

15. **(Twice Amended)** A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence at least 80% identical to the C-terminal seven-cysteine skeleton of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.

B7

16. **(Twice Amended)** A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence at least 90% identical to the C-terminal seven-cysteine skeleton of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.

B7

17. **(Twice Amended)** A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence identical to the C-terminal seven-cysteine skeleton of human OP-1.

18. **(Twice Amended)** A method as in claim 1, wherein said OP/BMP morphogen is selected from OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6 and BMP9.

B7 C8

19. **(Amended)** A method as in claim 1, wherein said effective concentration of the preparation is between 0.1 ng/ml and 10 µg/ml of said OP/BMP morphogen and between 0.1 ng/ml and 10 µg/ml of said GDNF/NGF neurotrophic factor.

20. **(Reiterated)** A method as in claim 19 wherein, said effective concentration is between 1 ng/ml and 100 ng/ml of said OP/BMP morphogen.

21. **(Reiterated)** A method as in claim 19, wherein said effective concentration is between 1 ng/ml and 100 ng/ml of said GDNF/NGF neurotrophic factor.

22. **(Reiterated)** A method as in claim 19, wherein said effective concentration is between 1 ng/ml and 100 ng/ml of said OP/BMP morphogen and between 1 ng/ml and 100 ng/ml of said GDNF/NGF neurotrophic factor.

B7 E7

23. **(Amended)** A method as in claim 1, wherein said GDNF/NGF neurotrophic factor comprises GDNF.

DW C10

28. (Twice Amended) A pharmaceutical preparation for promoting the survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence at least 70% identical to the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

B9

29. (Twice Amended) A pharmaceutical preparation for inhibiting the death or degeneration of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence at least 70% identical to the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

The claims presented above incorporate changes as indicated by the marked-up version below.

1. (Twice Amended) A method for promoting survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine theronine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

contacting neural cells with an effective concentration of a preparation comprising

(a) an OP/BMP morphogen having an amino acid sequence ~~with~~ at least 70%

~~identical to homology with~~ the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone, and

(b) a GDNF/NGF neurotrophic neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6.

11. (Amended) A method as in claim 1, ~~any one of claims 1-4~~ wherein said neural cells comprise neurons or neurological cells.
13. (Amended) A method as in claim 1, ~~any one of claims 1-4~~ wherein said neural cells comprise peripheral nervous system cells.
15. (Twice Amended) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence ~~having at least 80% identical to 80% homology with~~ the C-terminal seven-cysteine skeleton domain of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.
16. (Twice Amended) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence ~~having at least 90% identical to 60% amino acid identity with~~ the C-terminal seven-cysteine skeleton domain of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.
17. (Twice Amended) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence ~~having at least identical to 70% amino acid identity with~~ the C-terminal seven-cysteine skeleton domain of human OP-1.
18. (Twice Amended) A method as in claim 1, wherein said OP/BMP morphogen ~~comprises at least the C-terminal six or seven cysteine domain of a mammalian protein~~ is selected from the group consisting of OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6 and BMP9.
19. (Amended) A method as in claim 1, ~~any of claims 1-4~~ wherein said effective concentration of the preparation is between 0.1 ng/ml and 10 µg/ml of said OP/BMP morphogen and between 0.1 ng/ml and 10 µg/ml of said GDNF/NGF neurotrophic factor.
23. (Amended) A method as in claim 1, ~~any of claims 1-4~~ wherein said GDNF/NGF neurotrophic factor comprises a mature, functional form of a protein ~~selected from the group consisting of~~ GDNF NGF, BDNF, NT-3, NT-4, NT-5 and NT-6.

28. (Twice Amended) A pharmaceutical preparation for promoting the survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence at least 70% identical to the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

29. (Twice Amended) A pharmaceutical preparation for inhibiting the death or degeneration of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/ threonine threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence at least 70% identical to the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

REMARKS

Claims 1-13 and 15-29 constitute the pending claims in the present application, and claims 1, 11, 13, 15-24, 28 and 29 are currently under consideration having been elected with traverse. Applicants will cancel non-elected claims upon the indication of allowable subject matter. Applicants cancel, without prejudice, claim 24. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Applicants note that the Group and/or Art Unit of this application has changed.

Applicants will address this and all future correspondence to Regina M. DeBerry, Group Art Unit 1647.